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The association between diet and physical activity on insulin resistance in the Women's Interagency HIV Study

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Abstract

Objectives—To evaluate the association of diet and physical activity with insulin resistance (IR) in HIV-infected and uninfected women.

Methods—Cross sectional analyses of summary dietary measures and physical activity intensity scores obtained from women enrolled in the San Francisco (n=113) and Chicago (n=65) Women's Interagency HIV Study (WIHS) sites. IR was estimated using the homeostasis model assessment (HOMA-IR). Stepwise regression models assessed the association of diet and physical activity with HOMA-IR after adjustment for demographic, behavioral, and clinical factors.

Results—Compared to HIV-uninfected women, HIV-infected women were older and more likely to have health insurance. In multivariable analysis including all women, being from San Francisco (p=0.005), having a higher mean body mass index (BMI, p<0.001), and a higher percent kilocalories from sweets (p=0.025) were associated with greater HOMA-IR; heavy intensity physical activity (p=0.006) and annual household income <$36,000 (p=0.002) was associated with a lower HOMA-IR. In analysis limited to HIV-infected women, having a higher BMI (p<0.001) and a history of protease inhibitor use (0.002) were significantly associated with higher HOMA-IR; heavy intensity activity (p=0.06) was marginally associated with lower HOMA-IR and being menopausal (p=0.05) was marginally associated with higher HOMA-IR.

Conclusions—Among urban women with or at risk for HIV-infection, heavy intensity physical activity was associated with lower HOMA-IR while higher percent kilocalories from sweets were associated with higher HOMA-IR. Given the overall health benefits of physical activity and a diet low on sugar, these behaviors should be encouraged whenever possible.

Keywords

HIV; HOMA-IR; insulin resistance; macronutrients; physical activity; women

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INTRODUCTION

Disorders of glucose metabolism are common in HIV infection and of concern due to the increased risk of cardiovascular disease.(1-3) Prior studies in the Women's Interagency HIV Study (WIHS) found that HIV-infected women on highly active antiretroviral therapy (HAART) had greater insulin resistance (IR) than HIV-uninfected women and, among HIV-infected women, longer cumulative exposure to NRTI, especially stavudine, was associated with greater IR.(4) This study also found that family history of diabetes, hepatitis C virus seropositivity, higher body mass index (BMI), and self-reported menopause were each independently associated with greater IR.

Few studies have examined how modifiable risk factors such as diet and exercise may affect IR in the setting of HIV infection. This investigation used a subset of HIV-infected and uninfected women from the WIHS and examined the associations of diet and physical activity with IR estimated using the homeostasis model assessment (HOMA-IR). Our hypothesis was that a healthy diet (low in carbohydrates and sweets) and moderate to heavy physical activity would be associated with lower HOMA-IR after controlling for HIV and non-HIV related IR factors.

METHODS

Study population

Data from two centers of the United States WIHS were used for this investigation, San Francisco, California, and Chicago, Illinois. In brief, recruitment of HIV-infected and uninfected women into the WIHS occurred in 1994-1995 and again in 2001-2002, for a total of 797 HIV-infected and 252 HIV-uninfected women at these two centers combined. Women were seen for core study visits twice a year and data were collected with a standardized interview-based questionnaire. Detailed information about the WIHS study methodology, quality assurance, and baseline characteristics of enrollees can be found in previously published literature.(5, 6) Study protocols were reviewed and approved by the institutional review boards, and written informed consent was obtained from all participants.

During WIHS visits 20-23 (April 2004 through March 2006), 275 women from the San Francisco and Chicago WIHS sites were administered the Brief Block Food Frequency Questionnaire.(7) This dietary questionnaire was originally developed by the National Cancer Institute, has been extensively studied and validated, and is designed to be self-administered but participants who wanted assistance completing the survey were helped. The questionnaire asks about the number of days each food item was consumed in the past week and the average portion size consumed on those days; pictures were provided to enhance the accuracy of reporting on portion size. Results include the average intake and the recommended levels of 1) macronutrients - calories, fat, saturated fat, monounsaturated fat, polyunsaturated fat, percent of calories from fat, protein, carbohydrates, cholesterol, fiber; 2) antioxidants - vitamin A, beta-carotene, vitamin C, vitamin E; 3) B-vitamins - Vitamin B1, B2, folic acid, B6, niacin; 4) minerals - calcium, sodium, potassium, iron, zinc; 5) food group servings - fruits, vegetables, dairy, meats, grains, fats & sweets; and 6) nutrients from vitamin supplements (if taken).

In addition and during those same visits, physical activity was assessed in 523 women using a questionnaire which has been validated in the Coronary Artery Risk Development in Young Adults (CARDIA) study (8) and used by the multi-site study of Fat Redistribution And Metabolic changes in HIV infection (FRAM).(9) In brief, the Physical Activity History questionnaire categorized participation in 13 activities during the previous yearinto three groups based on intensity; moderate intensity (walking, bowling, etc), heavy intensity (running, biking, etc), and total intensity (the sum of all types of activities).

For these analyses, WIHS visits were selected if both diet and physical activity data were available. Of these 255 women, 25 were excluded due to missing data on IR. Of the remaining 230 women, 52 had missing laboratory data or prevalent diabetes mellitus (DM) (defined as a fasting glucose ≥ 126 mg/dL or hemoglobin A1C ≥ 6.5 or self-reported DM or self-reported anti diabetic medication use, all at or before the index visit) and were excluded from the analyses. Our final study population consisted of 178 women, 122 out of 797 (15%) HIV-infected and 56 out of 252 (22%) uninfected participants.

Insulin resistance was estimated using the HOMA-IR and defined as (insulin × glucose)/405 with insulin measured in μIU/mL and glucose measured in mg/dL.(10) Fasting specimens for glucose determination were collected in tubes with glycolytic inhibitors and serum for insulin determination was obtained at the same time; all specimens were stored at −70°C until the day of assay and all specimens were tested at a central laboratory.

The dietary measures we evaluated were the macronutrients since these are more likely to be associated with IR; these included the average daily intake 1) percent of kilocalories (kcal) from carbohydrates, 2) percent of kcal from fat, 3) percent kcal from protein, 4) percent kcal from sweets (Block defines sweets as cookies, cakes, pies, donuts, candy, ice cream, sweetened cereals, and chocolate beverages), and 5) percent kcal from alcoholic beverages. Physical activity intensity scores were calculated (moderate, heavy, and total) and used as continuous variables in the analyses.(8)

Other variables included in the analyses were HIV infection, WIHS site, age, race/ethnicity, educational attainment, average household income, and health insurance. Health factors that were assessed included depressive symptoms (a binary indicator of a score of 16 or higher on the Center for Epidemiological Studies Depression (CES-D) Scale)20, smoking status, use of marijuana in the past 6 months, individual indicators of crack, cocaine, methadone, or heroin use (yes or no within the past 6 months), indicators of alcohol use in the past 6 months, menses in the past 12 months, total number of live born children, family history of DM, active hepatitis C virus (HCV) infection (defined by a detectable serum HCV RNA), and BMI (kg/m^2). For the HIV-infected women only, the following variables were evaluated; use of HAART,(11) history of protease inhibitor (PI) use, history of nucleoside reverse transcriptase inhibitor (NRTI) use, CD4+ T cell count, and plasma HIV RNA load.

Statistical Analysis

The primary dependent variable for this analysis was HOMA-IR and the primary independent variables were summary dietary measures and physical activity intensity scores. Contingency table analyses were performed to compare the distribution of participant characteristics by HIV status, and *P* values were based on chi-square or Fisher exact tests. For the regression analyses, HOMA-IR was log transformed to improve normality and correct for outliers. For the same reason, the activity intensity scores variables were log-transformed for the regression models. Unadjusted analyses were performed by linear regression between the log-transformed outcome and the categorical or continuous variables of interest. Since HOMA-IR was log-transformed, the results are back-transformed to produce estimated percentage differences in HOMA-IR attributable to each factor. Multivariable models were constructed by stepwise regression using backward elimination until all predictors had a p-value of less than 0.10. Each candidate model was run separately to avoid excessive case-wise deletion of observations that had missing values on other unselected candidate predictors. When the final models were selected (one model for all women and one model for the HIV-infected women only), all other risk factors were added one at a time to determine the adjusted risk, 95% CI, and p-values for that particular variable. Statistical analyses were performed using SAS® software version 9.2.(12)

RESULTS

The 178 participants included in these analyses did not significantly differ from the rest of the WIHS cohort in terms of HIV status, age, level of education, average income, or BMI. Compared to the women not in this study, women in this study were more likely to be African American (65% v. 59%, p=0.002) and had lower HOMA-IR (p<0.001). The HIV-infected women in the study were also similar to the HIV-infected women in the rest of the WIHS cohort in regard to CD4+ cell count and HIV viral load, but were less likely be on HAART (58% v. 67%, p=0.03).

In this study and compared to HIV-uninfected women, HIV-infected participants were older and to have health insurance. There were no significant differences between HIV-infected and uninfected women by HOMA-IR, physical activity, or any of the dietary measures (Table 1). Women with higher BMI were more likely to be HIV-uninfected (p=0.03), multiparous (p=0.01), HCV RNA negative (p=0.02), and have higher HOMA-IR (p=0.001).

Factors associated with HOMA-IR were similar in unadjusted and adjusted analyses of all 178 women (Table 2). In adjusted analyses, heavy intensity activity (p=0.006) and annual household income >$36,000 (p=0.02) were independently associated with lower HOMA-IR while being from San Francisco (p=0.005), having a higher BMI (p<0.001), and higher percent kcal from sweets (p=0.025) were associated with higher HOMA-IR.

In unadjusted analyses among the HIV-infected women only, we found that the inferences in unadjusted analysis were generally the same as for the pooled HIV-infected and uninfected group (Table 3); higher BMI (p=0.001), ever used PI therapy (p<0.001), and ever use NRTI therapy (p=0.004) was significantly associated with higher HOMA-IR. After adjustment, heavy intensity activity (p=0.06) was marginally associated with lower HOMA-IR, while having a higher BMI (p<0.001) and ever use of PI therapy (p=0.002) were associated with higher HOMA-IR and being menopausal (>12 months of amenorrhea, p=0.05) was marginally associated with higher HOMA-IR.

To further explore the relationship between BMI and HOMA-IR, we ran regression models and categorized BMI using standard cut points for underweight, normal weight, overweight and obese, and found evidence of a gradient (and not a threshold) between higher HOMA-IR and higher BMI (data not shown).

DISCUSSION

This is among the first studies to examine the association of diet and physical activity with IR in HIV-infected US women. Consistent with studies conducted in HIV-uninfected populations,(13-15) we demonstrated an association between heavy intensity physical activity and lower HOMA-IR in women with and at risk for HIV-infection. We also observed an association between higher percent of kcal from sweet intake and higher HOMA-IR, as has been reported in the literature.(16) These findings suggest that increased physical activity and diets low in sugar should be a focus of interventions to decrease HOMA-IR and the long term risk of DM and cardiovascular disease.

A possible mechanism by which high intensity activity decreases IR is through the decrease in the amount of visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) with exercise. The Fat Redistribution and Metabolic Change in HIV Infection (FRAM) study reported that increased physical activity was associated with decreased VAT and leg SAT in

HIV-infected men(17) and that the amount of VAT and upper trunk SAT was associated with HOMA-IR in both HIV-infected and uninfected adults.(18) Our results are consistent with those from the FRAM study, which reported that among HIV-uninfected men and women, vigorous activity was associated with a lower risk of IR.(18) We extend that finding to HIV-infected women. In aggregate, these studies suggest that physical activity programs could have a significant health impact in HIV-infected persons. By increasing exercise, the long term effects of cardiovascular risk factors might be ameliorated.

In our cohort of predominantly poor women, we found that annual income below $36,000 was associated with higher HOMA-IR. Studies in HIV-uninfected populations have also found lower income to be associated with metabolic syndrome.(19-21) Lower income may have been associated with fewer neighborhood resources for physical activity and healthy foods (as opposed to processed foods which may be more affordable). A prior study of adults in the Multi-Ethnic Study of Atherosclerosis reported that greater neighborhood physical activity resources and greater access to healthy food were consistently associated with lower HOMA-IR.(22) While increasing household income may not be a modifiable factor, improving access to neighborhood resources for physical activity and healthy foods is a worthy goal and might result in a decreased risk of DM and heart disease among residents in the neighborhood.

Prior studies of IR in the WIHS and the Multicenter AIDS Cohort Study (MACS) also reported that a higher BMI and, in the WIHS, PI use were associated with higher HOMA-IR among HIV-infected women and men, respectively.(4, 23) Our findings suggest that in addition to physical activity, other indicators of better health (i.e. normal weight and a healthy diet) is associated with lower HOMA-IR.

It is noteworthy that women from the San Francisco Bay Area site were more likely to have higher HOMA-IR than women from the Chicago site. These differences are not likely due to laboratory variation since glucose and insulin were tested in a centralized laboratory and run in batch. Chicago women were significantly younger and more likely to be African American than the women from the Bay Area, but when age and race were included in the stepwise models for HOMA-IR, women from the Chicago site remained at lower risk. Another possibility is that the African-American women had less visceral adipose tissue than the Caucasian women (24) and thus lower HOMA-IR, and since the Chicago women were more likely to be African-American this might contribute to our findings.

While hypertension and serum lipid abnormalities frequently accompany insulin resistance, we did not include measurements of serum lipids and blood pressure in these analyses because these factors are generally not a precursor, and thus not predictive of insulin resistance.(25) In fact there is evidence to the contrary, that insulin resistance might contribute to the development of hypertension and dyslipidemia.(26, 27)

Our study is not without limitations, for example this was a cross-sectional study and therefore we cannot determine a temporal relationship between our dependent and independent variables. In addition, we evaluated a subset of the WIHS and it is possible that women who consented to participate in this sub study were different from the total WIHS cohort. However, the characteristics of our study sample closely resemble that of the entire WIHS during the time under study.(28) Although our sample population was relatively small and may have limited power, we were still able to detect several significant factors associated with HOMA-IR. Lastly, we relied on self-reports of diet and physical activity and our participants may have under-reported their macronutrient intake and over-reported their physical activity; this bias would be towards the null of finding no association but we were still able to detect an association with heavy intensity activity and higher percent kcal from sweets. Despite these limitations the study has several strengths, including a racially representative sample of HIV-infected women in the United States with a well-matched comparison group.

In summary, in this study population of urban women with or at risk for HIV-infection, heavy intensity activity was associated with lower HOMA-IR while higher percent kilocalories from sweets were associated with higher HOMA-IR. Given the overall health benefits of physical activity and a diet low in concentrated sweets, these behaviors should be encouraged whenever possible. Additionally, diabetes and heart disease prevention efforts may need to consider features of residential environment, such as resources for physical activity and healthy foods.

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TABLE 1

Participant characteristics by HIV status for 178 women in the Women's Interagency HIV Study of diet and physical activity.

Characteristic	HIV-infected n (%)	HIV-uninfected n (%)	P-value
WIHS site			0.85
Chicago	44 (36)	21 (38)	
San Francisco	78 (64)	35 (63)	
Age (years)			0.004
≤30	8 (7)	14 (25)	
31-40	43 (35)	20 (36)	
41-50	43 (35)	13 (23)	
>50	28 (23)	9 (16)	
Race/Ethnicity			0.18
Non-Hispanic white	25 (20)	6 (11)	
African-American	78 (64)	37 (66)	
Other	19 (16)	13 (23)	
Level of education			0.30
Less than high school diploma	39 (32)	14 (25)	
High school diploma	45 (37)	18 (32)	
Some college or more	38 (31)	24 (43)	
Average income per year			0.42
<$12000	77 (64)	30 (54)	
$12001-$36000	32 (26)	18 (32)	
>$36000	12 (10)	8 (14)	
Not reported	1	0	
Health insurance	110 (90)	36 (64)	<0.001
CES-D[a] scale score ≥16	52 (43)	16 (29)	0.07
Current cigarette smoker	59 (49)	27 (48)	0.95
Marijuana use in the last 6 months	30 (25)	19 (34)	0.21
Illicit drug use[b] in the last 6 months	26 (21)	15 (27)	0.44
Alcohol use in the last 6 months			0.16
0 drinks/week	50 (42)	18 (32)	
<3 drinks/week	49 (41)	23 (41)	
3-13 drinks/week	18 (15)	15(27)	
>13 drinks/week	3 (3)	0	
Not reported	2	0	
Menses in the past 12 months	84 (66)	44 (77)	0.13
Number of live born children			0.86

Characteristic	HIV-infected n (%)	HIV-uninfected n (%)	P-value
0	29 (24)	15 (27)	
1-3	64 (52)	27 (48)	
>3	29 (24)	14 (25)	
Family history of diabetes	40 (37)	16 (31)	0.49
Hepatitis C RNA positivity	31 (27)	8 (15)	0.07
Body Mass Index, median (IQR)	26.2 (22.1-31.9)	29.4 (25.3-33.9)	0.06
HOMA-IR , median (IQR)	1.9 (1.2-3.3)	2.0 (1.1-3.5)	0.52
Heavy intensity activity, median (IQR)	49 (0-302)	81 (0-210)	0.39
Moderate intensity activity, median (IQR)	69 (4-172)	55 (16-144)	0.79
Total intensity activity, median (IQR)	124 (48-288)	173 (46-345)	0.18
Daily kilocalories (kcal) intake, median (IQR)	1795 (1111-3205)	1757(1111-3154)	0.52
% of kcal from carbohydrate, median (IQR)	48 (43-54)	49 (42-58)	1.0
% of kcal from fat, median (IQR)	36 (32-41)	36 (29-41)	1.0
% of kcal from protein, median (IQR)	14 (13-17)	14 (12-17)	0.52
% of kcal from sweets, median (IQR)	12 (5-23)	13 (6-25)	0.52
% of kcal from alcoholic beverages median (IQR)	0.1 (0-1.9)	0.1 (0-3.9)	0.97
CD4+ count (per mm^3), median (IQR)	409 (265-614)		
CD4+ count (per mm^3)			
<200	15 (12)		
200-499	63 (52)		
>500	44 (36)		
Viral load, median (IQR)	670 (80-8900)		
Viral load, copies			
<81	51 (42)		
81-3999	33 (27)		
4000-49999	28 (23)		
>49999	10 (8)		
Current HAART use	74 (61)		
History of PI use	66 (54)		
History of NRTI use	101 (83)		

[a]Center for Epidemiologic Studies Depression.

[b]Includes crack, cocaine, methadone, and/or heroin.

TABLE 2

Unadjusted and adjusted regression analyses, modeling log transformed HOMA-IR score among the 122 HIV-infected and 56 HIV-uninfected women in the Women's Interagency HIV Study of diet and physical activity.

Independent Variable	Sub-Category	Unadjusted Exponential beta (95% CI)	P-value	Adjusted[d] Exponential beta (95% CI)	P-value
HIV-infected		0.89 (0.68-1.15)	0.36	1.02 (0.80-1.28)	0.90
WIHS site	San Francisco	1.29 (1.00-1.65)	0.05	**1.39 (1.10-1.74)**	**0.005**
	Chicago [c]	1.0		**1.0**	
Age (per 10 years)		1.05 (0.94-1.19)	0.37	1.07 (0.96-1.19)	0.24
Race/Ethnicity	African-American	1.25 (0.98-1.61)	0.08	1.19 (0.92-1.52)	0.18
	All other [c]	1.0		1.0	
Education	No high school degree	1.34 (1.03-1.74)	0.03	1.25 (0.98-1.59)	0.07
	High school degree [c]	1.0		1.0	
Household income	≤$36000	0.64 (0.44-0.94)	0.02	**0.67 (0.47-0.95)**	**0.02**
	<$36000 [c]	1.0		**1.0**	
Health Insurance	Yes	1.07 (0.78-1.47)	0.66	1.04 (0.79-1.37)	0.79
	No[c]	1.0		1.0	
CES-D[a] Scale score	≥16	1.17 (0.91-1.50)	0.23	1.09 (0.86-1.37)	0.47
	<16[c]	1.0		1.0	
Ever smoker	Yes	1.05 (0.79-1.39)	0.73	1.05 (0.80-1.38)	0.71
	No[c]	1.0		1.0	
Marijuana use in the last 6 months	Yes	0.94 (0.69-1.30)	0.73	0.99 (0.73-1.33)	0.94
	No[c]	1.0		1.0	
Illicit drug use [b] in the last 6 months	Yes	1.06 (0.79-1.41)	0.71	1.04 (0.80-1.35)	0.79
	No[c]	1.0		1.0	
Alcohol use in the last 6 months	Yes	0.90 (0.70-1.15)	0.39	0.95 (0.76-1.19)	0.67
	No[c]	1.0		1.0	

Independent Variable	Sub-Category	Unadjusted Exponential beta (95% CI)	P-value	Adjusted[d] Exponential beta (95% CI)	P-value
Menses in the past 12	No	1.09 (0.84-1.42)	0.52	1.17 (0.91-1.49)	0.22
months	Yes[c]	1.0		1.0	
# of live born children		1.04 (0.98-1.10)	0.18	1.01 (0.95-1.06)	0.80
Family history of DM	Yes	1.12 (0.85-1.46)	0.42	1.11 (0.88-1.42)	0.38
	No[c]	1.0		1.0	
Hepatitis C RNA +	Yes	1.20 (0.89-1.61)	0.24	1.25 (0.94-1.65)	0.12
	No[c]	1.0		1.0	
BMI per 5 units		1.24 (1.15-1.34)	<0.001	**1.22 (1.14-1.32)**	**<0.001**
Log 2 moderate intensity activity		0.97 (0.93-1.01)	0.16	0.99 (0.94-1.03)	0.57
Log 2 heavy intensity activity		0.96 (0.92-0.99)	0.02	**0.95 (0.92-0.99)**	**0.006**
Log 2 total intensity activity		0.96 (0.92-1.00)	0.06	0.98 (0.92-1.04)	0.49
% kcal from carbohydrate,		1.01 (1.00-1.02)	0.10	1.00 (0.99-1.02)	0.43
% kcal from fat		1.00 (0.98-1.01)	0.71	1.00 (0.98-1.01)	0.53
% kcal from protein		0.98 (0.95-1.01)	0.21	1.01 (0.98-1.05)	0.48
% kcal from sweets		1.01 (1.00-1.02)	0.004	**1.01 (1.00-1.02)**	**0.025**
% kcal from alcoholic beverages		0.97 (0.95-1.00)	0.03	0.98 (0.96-1.01)	0.15

[a]Center for Epidemiologic Studies Depression

[b]Includes crack, cocaine, methadone, and/or heroin

[c]Reference group

[d]Model adjusted for WIHS site, household income, BMI, heavy intensity activity, and % kcal from sweets.

TABLE 3

Unadjusted and adjusted regression analyses modeling log transformed HOMA-IR score among the 122 HIV-infe women in the Women's Interagency HIV Study of diet and physical activity.

Independent Variable	Sub-Category	Unadjusted Exponential beta (95% CI)	P-value	Adjusted[d] Exponential beta (95% CI)	P-value
WIHS site	San Francisco	1.19 (0.90-1.58)	0.22	1.23 (0.94-1.60)	0.13
	Chicago[c]	1.0		1.0	
Age (per 10 years)		1.02 (0.89-1.17)	0.79	1.02 (0.87-1.19)	0.83
Race/Ethnicity	African-American	1.26 (0.95-1.67)	0.10	1.18 (0.89-1.56)	0.25
	All other[c]	1.0		1.0	
Education	No high school degree	1.16 (0.87-1.55)	0.31	1.13 (0.87-1.48)	0.36
	High school degree[c]	1.0		1.0	
Household income	>$36000	0.91 (0.57-1.44)	0.67	0.88 (0.58-1.35)	0.56
	≤$36000[c]	1.0		1.0	
Health Insurance	Yes	1.30 (0.83-2.06)	0.25	1.38 (0.92-2.06)	0.12
	No[c]	1.0		1.0	
CES-D[a] Scale score	≥16	1.10 (0.83-1.46)	0.51	1.17 (0.91-1.51)	0.22
	<16[c]	1.0		1.0	
Ever smoker	Yes	1.09 (0.78-1.52)	0.63	1.16 (0.84-1.60)	0.37
	No[c]	1.0		1.0	
Marijuana use in the last 6 months	Yes	1.12 (0.78-1.60)	0.54	1.27 (0.90-1.80)	0.18
	No[c]	1.0		1.0	
Illicit drug use[b] in the last 6 months	Yes	1.05 (0.76-1.47)	0.75	1.13 (0.83-1.53)	0.43
	No[c]	1.0		1.0	
Alcohol use in the last 6 months	Yes	1.05 (0.79-1.38)	0.75	1.04 (0.81-1.35)	0.74
	No[c]	1.0		1.0	
Menses in the past 12 months	No	1.21 (0.91-1.62)	0.19	**1.31 (1.00-1.73)**	**0.05**
	Yes[c]	1.0		**1.0**	

Independent Variable	Sub-Category	Unadjusted Exponential beta (95% CI)	P-value	Adjusted[d] Exponential beta (95% CI)	P-value
# of live born children		0.96 (0.90-1.03)	0.22	0.98 (0.92-1.05)	0.63
Family history of DM	Yes	1.13 (0.85-1.51)	0.40	1.07 (0.83-1.39)	0.59
	No[c]	1.0		1.0	
Hepatitis C RNA +	Yes	1.18 (0.85-1.62)	0.32	1.25 (0.91-1.72)	0.17
	No[c]	1.0		1.0	
BMI per 5 units		1.18 (1.07-1.29)	0.001	**1.21 (1.11-1.33)**	**<0.001**
Log2 moderate intensity activity		0.96 (0.92-1.01)	0.12	0.98 (0.94-1.03)	0.45
Log2 heavy intensity activity		0.97 (0.93-1.01)	0.10	**0.96 (0.93-1.00)**	**0.06**
Log 2 total intensity activity		0.97 (0.92-1.01)	0.13	0.98 (0.92-1.05)	0.63
% kcal from carbohydrate,		1.01 (1.00-1.03)	0.13	1.01 (1.00-1.02)	0.21
% kcal from fat		0.99 (0.98-1.01)	0.50	0.99 (0.98-1.01)	0.38
% kcal from protein		0.99 (0.96-1.03)	0.71	0.99 (0.69-1.02)	0.56
% kcal from sweets		1.01 (1.00-1.02)	0.13	1.01 (1.00-1.02)	0.11
% kcal from alcoholic beverages		0.98 (0.95-1.00)	0.08	0.99 (0.97-1.02)	0.49
CD4+ count (per 100 cells)		0.97 (0.92-1.02)	0.22	0.96 (0.91-1.02)	0.16
Log10 HIV viral load (copies)		0.99 (0.87-1.11)	0.82	1.03 (0.92-1.16)	0.61
Ever used HAART	Yes	1.28 (0.92-1.77)	0.14	0.88 (0.62-1.25)	0.46
	No[c]*	1.0		1.0	
Ever used PI	Yes	1.65 (1.28-2.15)	<0.001	**1.50 (1.17-1.93)**	**0.002**
	No[c]*	1.0		**1.0**	
Ever use NRTI	Yes	1.71 (1.19-2.44)	0.004	1.24 (0.84-1.81)	0.27
	No[c]*	1.0		1.0	

[a] Center for Epidemiologic Studies Depression

[b] Includes crack, cocaine, methadone, and/or heroin

[c] Reference group

[d]Mod adjusted for menopause, BMI, heavy intensity activity, and ever used PI.